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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/597,902	08/11/2006	Brian Alvin Johns	PR60567USW	7724
23347 7590 03/21/2008 GLAXOSMITHKLINE CORPORATE INTELLECTUAL PROPERTY, MAI B475 FIVE MOORE DR., PO BOX 13398 RESEARCH TRIANGLE PARK, NC 27709-3398				
EXAMINER				
ODELL, DAVID K				
ART UNIT		PAPER NUMBER		
1625				
NOTIFICATION DATE		DELIVERY MODE		
03/21/2008		ELECTRONIC		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

USCIPRTP@GSK.COM  
JULIE.D.MCFALLS@GSK.COM  
LAURA.M.MCCULLEN@GSK.COM

### Office Action Summary

**Application No.**

10/597,902

**Applicant(s)**

JOHNS ET AL.

**Examiner**

David K. O'Dell

**Art Unit**

1625

**Period for Reply** -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 05 February 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-21 and 25-40 is/are pending in the application.
- 4a) Of the above claim(s) 20, 21, 28-32, 35, 39 and 40 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-19, 25-27, 33, 34 and 36-38 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 11 August 2006
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

#### **DETAILED ACTION**

1. This application is a 371 of PCT/US05/04085 filed 02/10/2005, which claims benefit of 60/543,670 filed 02/11/2004.

Claims 1-21, 25-40 are pending.

#### ***Response to Restriction/Election***

2. Applicant's election of group I and the species 7-[(4- fluorophenyl)methyl]-4-hydroxy-N-(2-hydroxyethyl)-1-methyl-2-oxo-1,2-dihydro-1,5-naphthyridine-3-carboxamide in the reply filed on February 5, 2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP §818.03(a)). The applicant is correct in pointing out that the examiner misnumbered claim 32 as claim 24 in Group V (The process of preparing compounds of Formula 4h) in the restriction requirement. While this error is readily apparent, the Group V is reproduced below, for clarification. This application contains claims drawn to a nonelected invention with traverse. A complete reply to this action must include a cancellation of nonelected claims or other appropriate action.

Under examination:

Group I, Claims 1-19, 25-27, 33, 34, 36-38 drawn to compounds and compositions having a benzyl-naphthyridine-carboxamide core. If this group is elected, a further election of a single disclosed species of compound is also required. Further restriction based on the election may be made.

Group V clarified:

Group V, Claim 32, drawn to methods of making pyridines of Formula 4h. If this group is elected, a further election of a single disclosed species of 4h is also required. Further restriction based on the species election may be required.

### ***Title***

3. The title of the invention is not descriptive. The examiner has changed the title to "2-Oxonaphthyridine-3-carboxamides HIV Integrase Inhibitors", which is the title of the WIPO document of the 371 application from which this case claims lineage. If this is not acceptable suggestions may be made.

### ***Claim Rejections - 35 USC § 112 2<sup>nd</sup> paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-10, 19, 25-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim recites "C<sub>6</sub>-C<sub>14</sub> aryl". Based upon the definition in on pg. 7 of the specification an "aryl" is "refers to a carbocyclic aromatic moiety (such as phenyl or naphthyl) containing the specified number of carbon atoms, preferably from 6-14 carbon atoms, and more preferably from 6-10 carbon atoms. Examples of aryl radicals include, but are not limited to, phenyl, naphthyl, indenyl, azulenyl, fluorenyl, anthracenyl, phenanthrenyl." Presumably "C<sub>6</sub>-C<sub>14</sub> aryl" is meant to include compounds having 7, 9, 11, & 12 carbon atoms, however such compounds are not aromatic and thus conflict with the definition. For a discussion of aromaticity see Jones, M. *Organic Chemistry* Norton: New York, 1997, pgs. 578-591. The examiner believes this is meant to be phenyl and naphthyl.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference

claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-19, 25-27, 33, 34, 36-38 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11, 17-19 of copending Application No. 11/997,786. The claims are coextensive in scope. This is a provisional obviousness-type double patenting rejection.

Claims 1-19, 25-27, 33, 34, 36-38 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 5 of copending Application No. 11/478,218. The claims are coextensive in scope. This is a provisional obviousness-type double patenting rejection

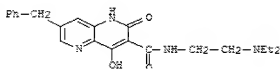
Claims 1-19, 25-27, 33, 34, 36-38 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 5, 12, 28 of copending Application No. 10/524,281 now a U.S. patent (number unknown). The claims are coextensive in scope. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

**Determination of the scope and content of the prior art and the instant claims**

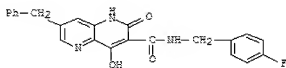
**(MPEP 2141.01)**

The '281 application teaches the compounds of the instant case, recites the compounds of the instant case. Where in claim 1, Formula I,  $R^1$  is H,  $R^2$  is H,  $R^3$  is alkyl substituted by  $N(R^a R^b)$ , where  $R^a$  and  $R^b$  are alkyl, the compounds shown below are produced:

RN 675614-21-3 CAPLUS  
CN 1,5-Naphthyridine-3-carboxamide, N-(2-(diethylamino)ethyl)-1,2-dihydro-4-hydroxy-2-oxo-7-(phenylmethyl)- {CA INDEX NAME}



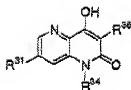
RN 675614-22-9 CAPLUS  
CN 1,5-Naphthyridine-3-carboxamide, N-((4-fluorophenyl)methyl)-1,2-dihydro-4-hydroxy-2-oxo-7-(phenylmethyl)- {CA INDEX NAME}



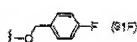
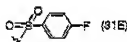
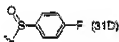
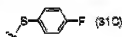
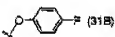
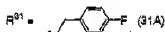
In addition these compounds have the same utility (HIV integrase inhibitor). It would appear that these compounds were invented by someone else. In addition Pg. 341 shows a description of other compounds, where R31 is 31A, R35 is 35F, 35G, 35H, and R34 is all of the definitions the compounds of the instant claims are produced. The examiner has provided a rough translation of the Japanese portion.

- 10 本発明化合物には、以下の化合物も含まれる。以下の化合物は上記実施例と同様に合成することができる。

Translation: Compounds of the present invention include,



上記化合物の  $R^{31}$ 、 $R^{34}$  及び  $R^{35}$  の置換基としては、以下の置換基が挙げられる。



$R^{34} =$  Me (34A), Et (34B), Pr (34C), COMe (34D), SO<sub>2</sub>Me (34E)

$R^{35} =$  COOMe (35A), COOEt (35B), COO<sup>i</sup>Pr (35C), OCEt (35D), COCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OMe (35E),  
CONHMe (35F), CONHEt (35G), CONHCH<sub>2</sub>CH<sub>2</sub>OMe (35H)

- 16 置換基の好ましい組合わせ ( $R^{31}$ ,  $R^{34}$ ,  $R^{35}$  として表わす) としては、以下の組合わせが挙げられる。

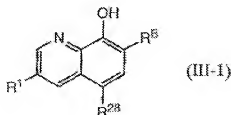
Translation: Preferably combinations of the substituents include the following

(31A, 34A, 35A), (31A, 34A, 35B), (31A, 34A, 35C), (31A, 34A, 35D), (31A, 34A, 35E), (31A, 34A, 35F), (31A, 34A, 35G), (31A, 34A, 35H), (31A, 34B, 35A), (31A, 34B, 35B), (31A, 34B, 35C), (31A, 34B, 35D), (31A, 34B, 35E), (31A, 34B, 35F),  
20 (31A, 34B, 35G), (31A, 34B, 35H), (31A, 34C, 35A), (31A, 34C, 35B), (31A, 34C, 35C, 341

35C), (31A, 34C, 35D), (31A, 34C, 35E), (31A, 34C, 35F), (31A, 34C, 35G), (31A, 34C, 35H), (31A, 34D, 35A), (31A, 34D, 35B), (31A, 34D, 35C), (31A, 34D, 35D), (31A, 34D, 35E), (31A, 34D, 35F), (31A, 34D, 35G), (31A, 34D, 35H), (31A, 34E, 35A), (31A, 34E, 35B), (31A, 34E, 35C), (31A, 34E, 35D), (31A, 34E, 35E), (31A, 34E, 35F), (31A, 34E, 35G), (31A, 34E, 35H),

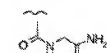
This would appear to be a case of anticipation as in *In re Schauman*, 572 F.2d 312, 197 USPQ 5 (CCPA 1978) or *In re Petering*, 301 F.2d 676, 133 USPQ 275 (CCPA 1962).

In addition to anticipatory species, the document also provides additional evidence for the obviousness of additional claims. In particular where in the instant case R1 is halogen or hydrogen, R2 is alkyl, sulfone, ketone or hydrogen, and R3 is alkyl or alkylamino or alkylalkoxy. Moreover the substituents on the bioisosteric quinolines also disclosed in this document on pg. 20. This position is referred to as R<sub>28</sub> in structure III-1 below:





This corresponds to the R2 position of the instant claims. The structure of the R28 groups are shown below (From pg. 21):



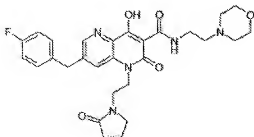
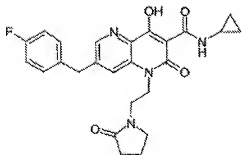
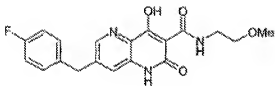
*Ascertainment of the difference between the prior art and the claims*

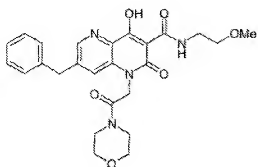
*(MPEP 2141.02)*

The instant claims are anticipated, but their may be some proviso attempting to remove some of the teaching of the reference. It is unclear what this proviso means, but nonetheless this proviso does nothing to the question of obviousness.

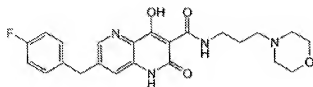
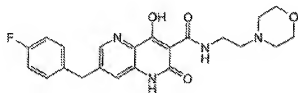
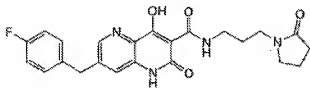
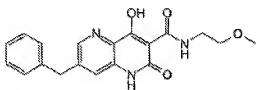
Comparing the instantly claimed preferred compounds (those with biological data), Below:

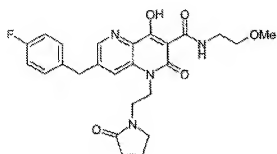
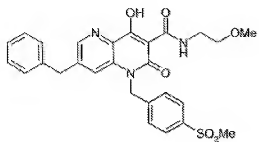
Example 2



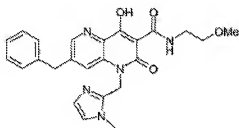


Example 17:

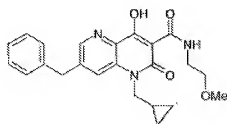




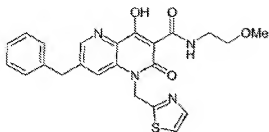
Example 50:



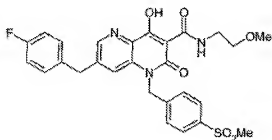
Example 54:



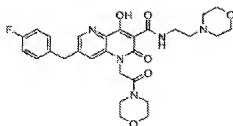
Example 62:



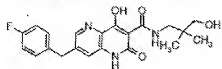
Example 64:



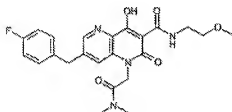
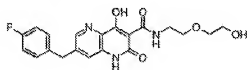
Example 83:



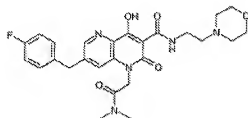
Example 85:



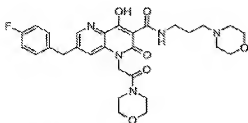
Example 86:



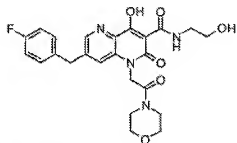
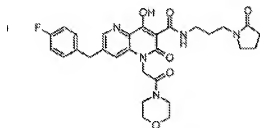
Example 91:



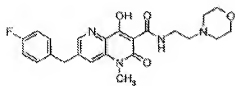
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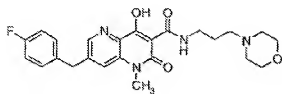


Example 94:

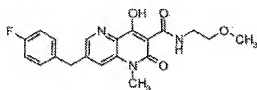


Example 96:

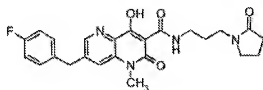




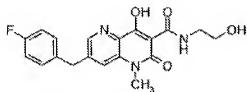
Example 98:



25 Example 99:

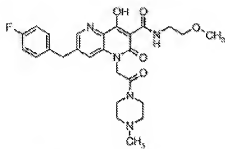


Example 101:

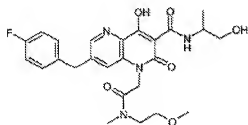
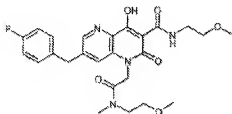




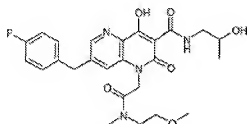
Example 102:



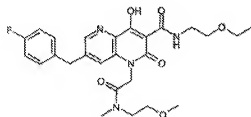
Example 104:



Example 106:



Example 107:



It is clear that all these substitutions were within the teaching of the claimed invention in the '281 application, in particular when R28 is considered.

**Finding of prima facie obviousness**

***Rational and Motivation***

***(MPEP 2142-2143)***

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to make compounds of the copending to produce the instant invention. The experienced Ph.D. synthetic organic chemist, who would make Applicants' compounds, would be motivated to prepare these compounds on the expectation that anticipatory compounds or

analogues falling within the general teaching would have similar properties and upon the routine nature of such experimentation in the art of medicinal chemistry.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

One of ordinary skill is also one of "ordinary creativity, not an automaton". See *Leapfrog Enterprises Inc. v. Fisher-Price. and Mattel Inc.* UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT "An obviousness determination is not the result of a rigid formula disassociated from the consideration of the facts of a case. Indeed, the common sense of those skilled in the art demonstrates why some combinations would have been obvious where others would not. See *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. , 2007 U.S. LEXIS 4745, 2007 WL 1237837, at 12 (2007) ("The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.").

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-10, 19, 25-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for certain compounds, does not reasonably provide enablement for the protracted list of compounds bearing the protracted list of substituents. The specification does not enable any person skilled in the art to which it pertains, or with which it is

most nearly connected, to make or use the invention commensurate in scope with these claims. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to the following:

- (A) *The breadth of the claims;*
- (B) *The nature of the invention;*
- (C) *The state of the prior art;*
- (D) *The level of one of ordinary skill;*
- (E) *The level of predictability in the art;*
- (F) *The amount of direction provided by the inventor;*
- (G) *The existence of working examples; and*
- (H) *The quantity of experimentation needed to make or use the invention*

In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

**(A) The breadth of the claims:** The claims are very broad encompassing all of heterocycles, carbocycles, and "aryls" bearing multiple substitutions **(B) The nature of the invention:** This is a medicinal chemistry invention requiring the synthesis of compounds and the compounds must have the utility as HIV integrase inhibitors. **(D) The level of one of ordinary skill:** One of ordinary skill is a medicinal chemist. **(C) The state of the prior art; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention:** It does seem highly probable that a high level variability on R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> (of Formula 1) can be achieved synthetically. However the most important limitations are those required for activity at the HIV integrase target. For R<sub>1</sub> the only information we have is for limited substituents (H, alkoxy and Fluorine). Despite the very large number of compounds disclosed in the specification, the structures are relatively homogenous. The data disclosed are shown below:

Compounds of the present invention have anti-HIV activity in the range  $IC_{50} \approx$   
1-1000 nM.

# Results

Compounds of the present invention have anti-HIV activity in this assay in the  
10 range  $IC_{50} \approx 1 - 1000$  nM.

Table 1:  $IC_{50}$  values for representative compounds

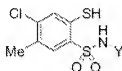
	Example number	$IC_{50}$ (nM)
	2	a*
15	9	a
	10	a
	12	a
	17	b**
	28	a
20	36	a
	37	a
	45	a
	49	a
	50	a
25	54	a
	62	a
	64	a
	83	b
	84	a
30	85	a
	86	a
	89	a
	91	b
	93	b

94	b
95	b
96	a
97	a
98	a
99	a
101	a
102	a
104	a
105	a
106	a
107	a
124	a
162	a
200	a
237	a
428	a
429	a
465	a
467	a
516	a
576	a

\*  $IC_{50} < 10 \text{ nM}$

\*\*  $IC_{50} = 10 - 25 \text{ nM}$

The examiner is mainly taking issue with the claim to "aryl" "heterocycle". The number of examples does not support the scope of the claims. While a few heterocycles were exemplified such as morpholine, piperazine, imidazole, thiazole, pyrrolidine and tetrahydropyran the substitution of one heterocycle for another is well known to have a large impact on the inhibitory activity of the compounds at HIV integrase. Zdzisław Brzozowski et. al. "Synthesis, anti-HIV-1 integrase, and cytotoxic activities of 4-chloro-N-(4-oxopyrimidin-2-yl)-2-mercaptobenzenesulfonamide derivatives" *European Journal of Medicinal Chemistry* **2007** in press doi:10.1016/j.ejmech.2007.08.013.



**13-20** [25]

Compd	X	Y
<b>8, 19</b>		
<b>9,20</b>		

Table 1

Anti-HIV integrase activity of novel 4-chloro-2-mercaptobenzenesulfonamide derivatives **13-28** and **35-44** and the reference 4-chloro-*N*-(3-amino-1*H*-1,2,4-triazol-5-yl)-2-mercapto-5-methylbenzenesulfonamide (NSC 661073) [24]

Compd	IC <sub>50</sub> <sup>a</sup> (μM)	
	3'-processing	Strand transfer
<b>13</b>	>100	>100
<b>14</b>	>100	>100
<b>15</b>	69 ± 6	43 ± 2
<b>16</b>	65 ± 2	53 ± 3
<b>17</b>	60 ± 12	35 ± 2
<b>18</b>	>100	81 ± 9
<b>19</b>	55 ± 5	39 ± 2
<b>20</b>	>100	>100

It is clear that replacing one heterocycle for another leads to unpredictable behavior (fused thiophene 19 for fused pyrazole 20 led to inactive compounds. In compounds related to those of the instant case SAR of heterocycle substitution on the amide group (perhaps corresponding to the R<sup>2</sup> position of the instant case), revealed a profound impact on activity. Alessia Petrocchi et. al. "From dihydroxypyrimidine carboxylic acids to carboxamide HIV-1 integrase inhibitors: SAR around the amide moiety" *Bioorganic & Medicinal Chemistry Letters* **2007**, 17, 350–353. "Efforts aimed at replacing the phenyl ring with a heterocycle are shown in Table 2. Compounds bearing polar heterocycles were completely inactive (17, 18, and 19). Substitution of the phenyl ring with thiophene (20) or with thiazoles (21 and 22) produced less active compounds. Potency was improved 10-fold and 2-fold, respectively, for benzothiophenes 23 and 24, and 5-fold for indole 25 confirming the presence of enough space."

Table 2. SAR at the heteroaryl amide

Compound	R <sup>2</sup>	QUICKIN IC <sub>50</sub> <sup>a</sup> (nM)
17	4-Pyridine	16,600
18	1 <i>H</i> -1,2,4-Triazole	50,000
19	1 <i>H</i> -Imidazole	17,000
20	2-Thiophene	100
21	2-(1,3-Thiazole)	200
22	5-(1,3-Thiazole)	2500
23	2-Benzothiophene	10
24	3-Benzothiophene	50
25	3-1 <i>H</i> -Indole	20

<sup>a</sup> HIV strand transfer assay, see Ref. 4.

The factors outlined in *In Re Wands* mentioned above apply here, and in particular As per the MPEP 2164.01 (a): "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification , at the time the application was filed,



would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).” It is very clear that one could not make/use this very broad invention that has few working examples in this unpredictable art without undue experimentation.

### *Conclusion*

5. No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David K. O'Dell whose telephone number is (571)272-9071. The examiner can normally be reached on Mon-Fri 7:30 A.M.-5:00 P.M EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Primary examiner, Rita Desai can be reached on (571)272-0684. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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D.K.O.

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Primary Examiner, Art Unit 1625